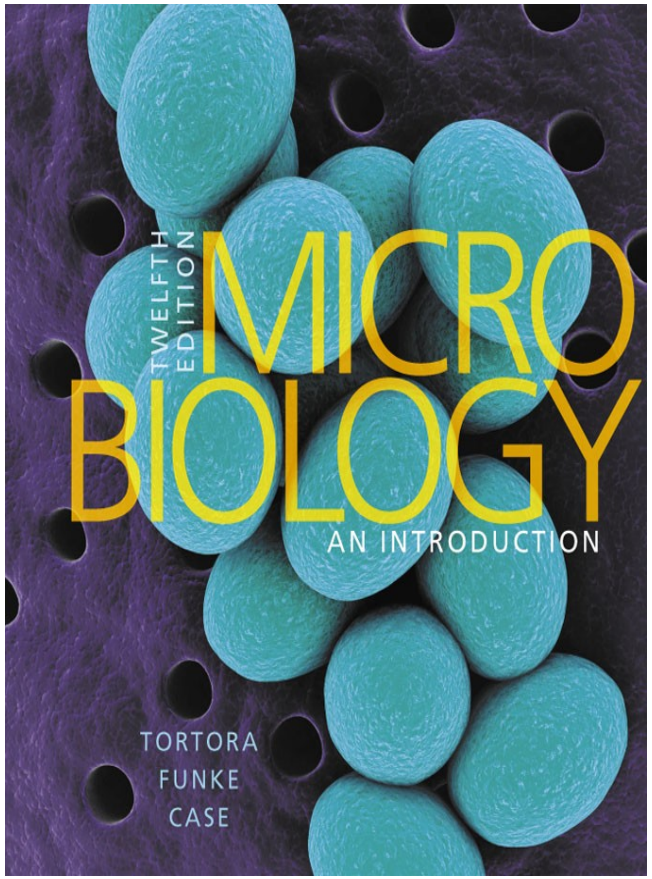
Microbiology an Introduction

Twelfth Edition



Chapter 15

Microbial Mechanisms of Pathogenicity

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Burkholderia Species

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How Microorganisms Enter a Host (1 of 3)

Learning Objectives

15-1 Identify the principal portals of entry.

15-2 Define **ID_{50}** and **LD_{50}.**

15-3 Using examples, explain how microbes adhere to host cells.

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How Microorganisms Enter a Host (2 of 3)

- **Pathogenicity:** the ability to cause disease
- **Virulence:** the degree of pathogenicity

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How Microorganisms Enter a Host (3 of 3)

- **Portals of entry**
  - Mucous membranes
  - Skin
  - Parenteral route
    - Deposited directly into tissues when barriers are penetrated
- Most pathogens have a preferred portal of entry

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Numbers of Invading Microbes
(1 of 3)

- **ID_{50}:** infectious dose for 50% of a sample population
  - Measures virulence of a microbe
- **LD_{50}:** lethal dose for 50% of a sample population
  - Measures potency of a toxin

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Numbers of Invading Microbes
(2 of 3)

Bacillus anthracis

Portal of Entry	ID_{50}
Skin	10–50 endospores
Inhalation	10,000–20,000 endospores
Ingestion	250,000–1,000,000 endospores

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Numbers of Invading Microbes
(3 of 3)

Toxins

Portal of Entry	ID_{50}
Botulinum	0.03 ng/kg
Shiga toxin	250 ng/kg
Staphylococcal enterotoxin	1350 ng/kg

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Adherence

- Almost all pathogens attach to host tissues in a process called **adherence** (**adhesion**)
- **Adhesins** (**ligands**) on the pathogen bind to **receptors** on the host cells
  - Glycocalyx
  - Fimbriae
- Microbes form **biofilms** (communities that share nutrients)

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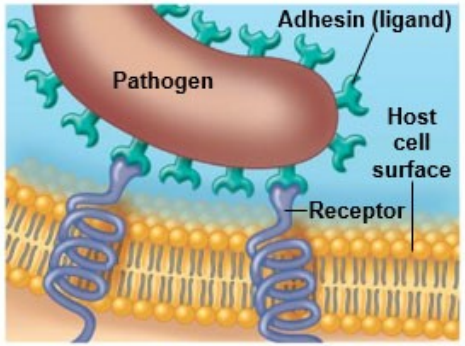
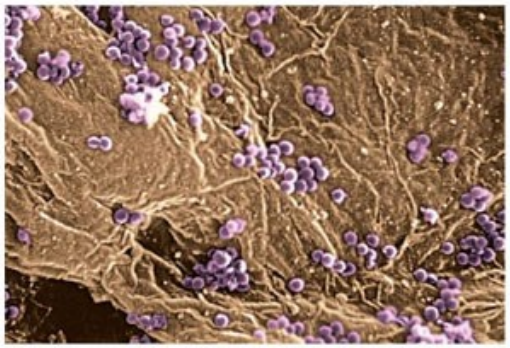
Figure 15.1 Adherence



(a) Surface molecules on a pathogen, called adhesins or ligands, bind specifically to complementary surface receptors on cells of certain host tissues.

(b) *E. coli* bacteria (yellow-green) on human urinary bladder cells SEM 1 μm



(c) Bacteria (purple) adhering to human skin SEM 9 μm

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Check Your Understanding-1

Check Your Understanding

- ✓ List three portals of entry, and describe how microorganisms gain access through each.
  15-1
- ✓ The LD_{50} of botulinum toxin is 0.03 ng/kg; the LD_{50} of **Salmonella** toxin is 12 mg/kg. Which is the more potent toxin?
  15-2
- ✓ How would a drug that binds mannose on human cells affect a pathogenic bacterium?
  15-3

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How Pathogens Penetrate Host Defenses

Learning Objectives

15-4 Explain how capsules and cell wall components contribute to pathogenicity.

15-5 Compare the effects of coagulases, kinases, hyaluronidase, and collagenase.

15-6 Define and give an example of **antigenic variation.**

15-7 Describe how bacteria use the host cell's cytoskeleton to enter the cell.

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Capsules

- Glycocalyx around the cell wall
- Impair phagocytosis
  - **Streptococcus pneumoniae**—pneumonia
  - **Haemophilus influenzae**—pneumonia and meningitis
  - **Bacillus anthracis**—anthrax
  - **Yersinia pestis**—plague

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Cell Wall Components

- **M protein** resists phagocytosis
  - **Streptococcus pyogenes**
- **Opa** protein allows attachment to host cells
  - **Neisseria gonorrhoeae**
- **Waxy lipid** (mycolic acid) resists digestion
  - **Mycobacterium tuberculosis**

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Enzymes

- **Coagulases:** coagulate fibrinogen
- **Kinases:** digest fibrin clots
- **Hyaluronidase:** digests polysaccharides that hold cells together
- **Collagenase:** breaks down collagen
- **IgA proteases:** destroy IgA antibodies

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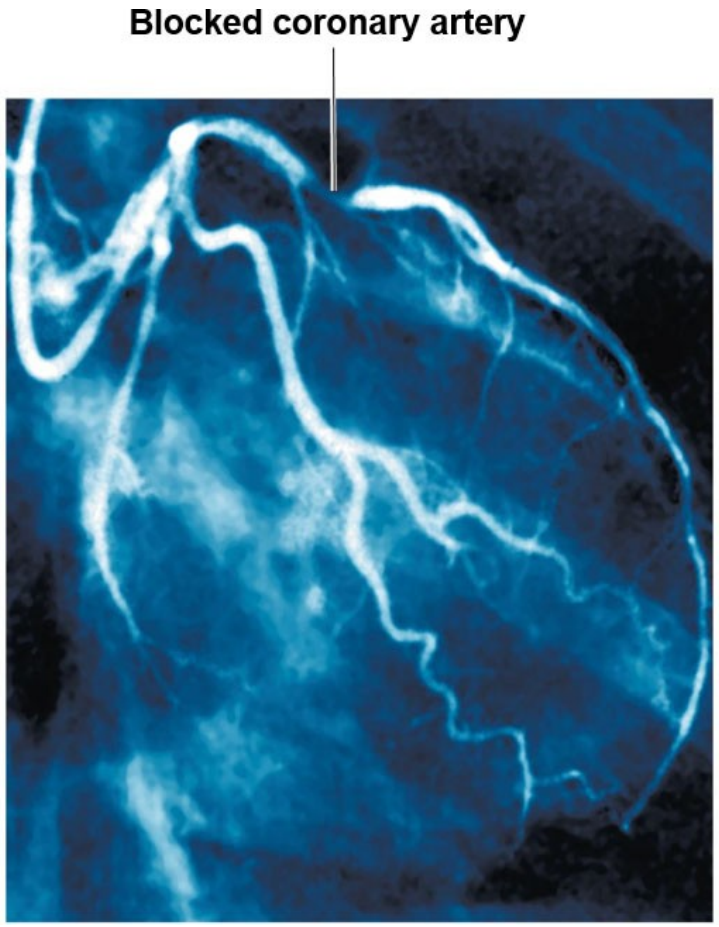
Applications of Microbiology 15.1a



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Applications of Microbiology 15.1b

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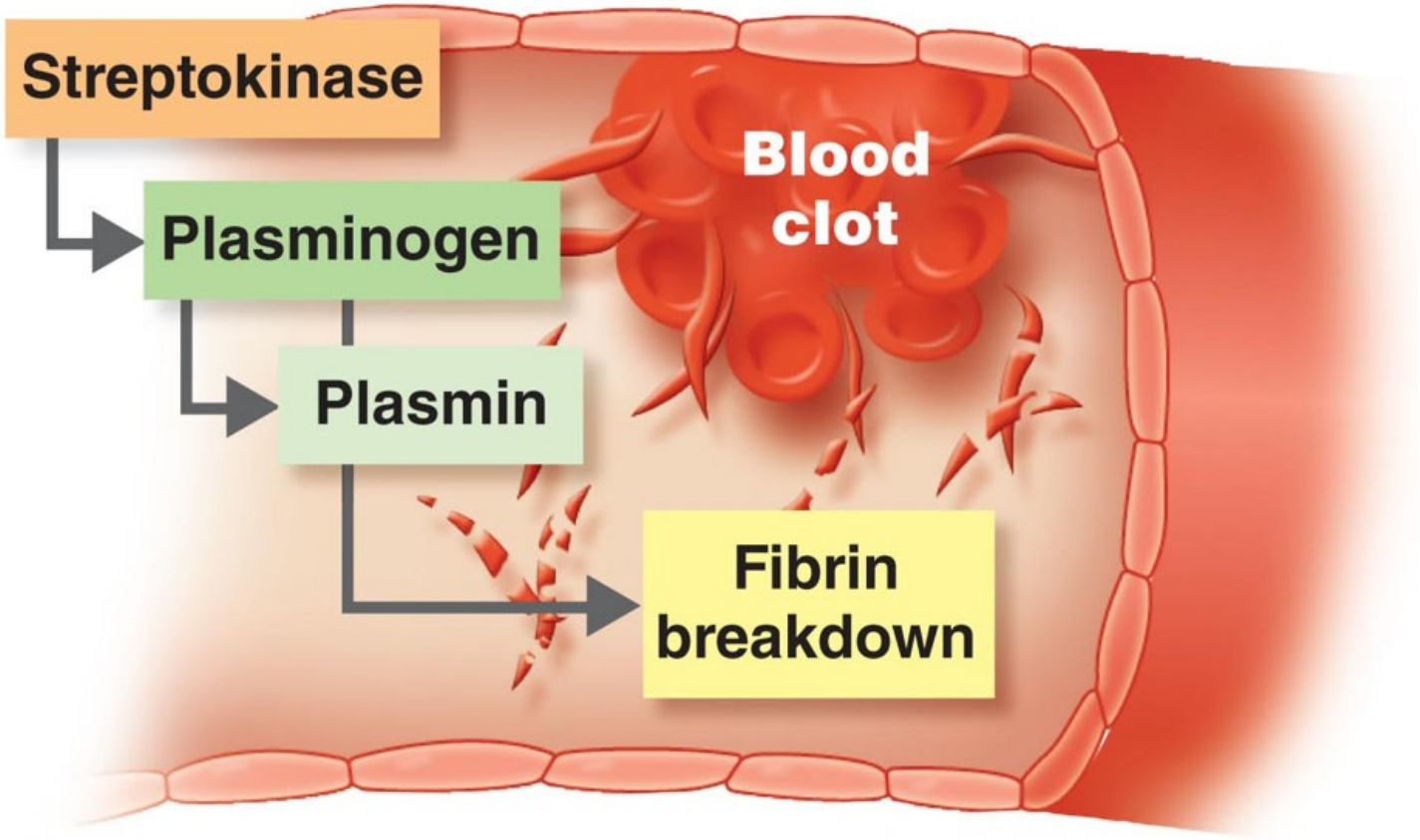
Applications of Microbiology 15.1c



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Antigenic Variation

- Pathogens alter their surface antigens (and antibodies are rendered ineffective)

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Penetration into the Host Cell Cytoskeleton

- Invasins
  - Surface proteins produced by bacteria that rearrange actin filaments of the cytoskeleton
    - Cause membrane ruffling
- Use actin to move from one cell to the next
  - **Shigella** and **Listeria**

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Virulence Factors: Hiding from Host Defenses

Animation: Virulence Factors: Hiding from Host Defenses

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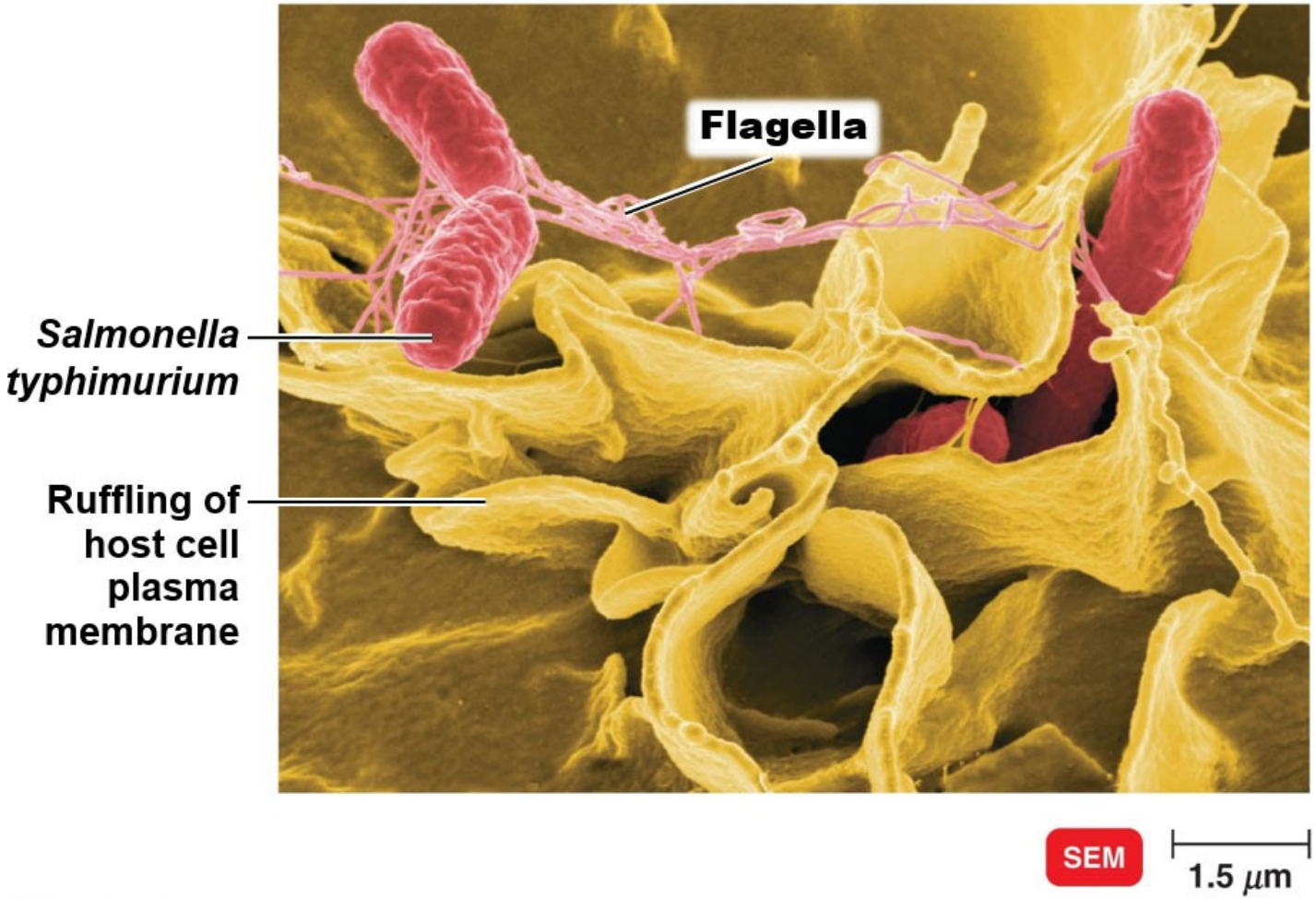
Figure 15.2 Salmonella Entering Intestinal Epithelial Cells as a Result of Ruffling



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Check Your Understanding-2

Check Your Understanding

- ✓ What function do capsules and M proteins have in common?
  15-4
- ✓ Would you expect a bacterium to make coagulase and kinase simultaneously?
  15-5
- ✓ Many vaccines provide years of protection against a disease. Why doesn't the influenza vaccine offer more than a few months of protection?
  15-6
- ✓ How does **Escherichia coli** cause membrane ruffling?
  15-7

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How Bacterial Pathogens Damage Host Cells (1 of 2)

Learning Objectives

15-8 Describe the function of siderophores.

15-9 Provide an example of direct damage, and compare this to toxin production.

15-10 Contrast the nature and effects of exotoxins and endotoxins.

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How Bacterial Pathogens Damage Host Cells (2 of 2)

Learning Objectives

15-11 Outline the mechanisms of action of A-B toxins, membrane-disrupting toxins, superantigens, and genotoxins.

15-12 Identify the importance of the LAL assay.

15-13 Using examples, describe the roles of plasmids and lysogeny in pathogenicity.

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Using the Host's Nutrients: Siderophores

- Iron is required for most pathogenic bacteria
- **Siderophores** are proteins secreted by pathogens that bind iron more tightly than host cells

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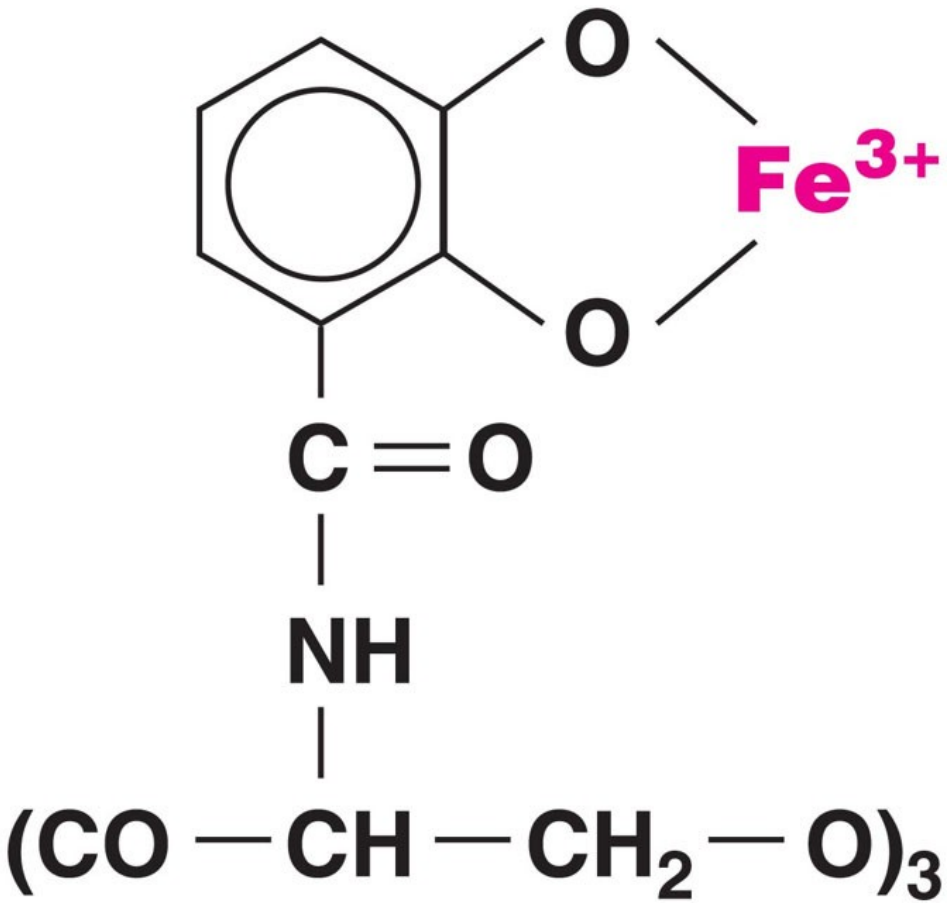
Figure 15.3 Structure of Enterobactin, One Type of Bacterial Siderophore



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Direct Damage

- Disrupts host cell function
- Uses host cell nutrients
- Produces waste products
- Multiplies in host cells and causes ruptures

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Virulence Factors: Penetrating Host Tissues

PLAY **Animation: Virulence Factors: Penetrating Host Tissues**

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Virulence Factors: Enteric Pathogens

Animation: Virulence Factors: Enteric Pathogens

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Production of Toxins

- **Toxins:** poisonous substances produced by microorganisms
  - Produce fever, cardiovascular problems, diarrhea, and shock
- **Toxigenicity:** ability of a microorganism to produce a toxin
- **Toxemia:** presence of toxin in the host's blood
- **Intoxications:** presence of toxin without microbial growth

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Exotoxins (1 of 6)

- Proteins produced and secreted by bacteria
  - Soluble in bodily fluids; destroy host cells and inhibit metabolic functions
- **Antitoxins:** antibodies against specific exotoxins
- **Toxoids:** inactivated exotoxins used in vaccines

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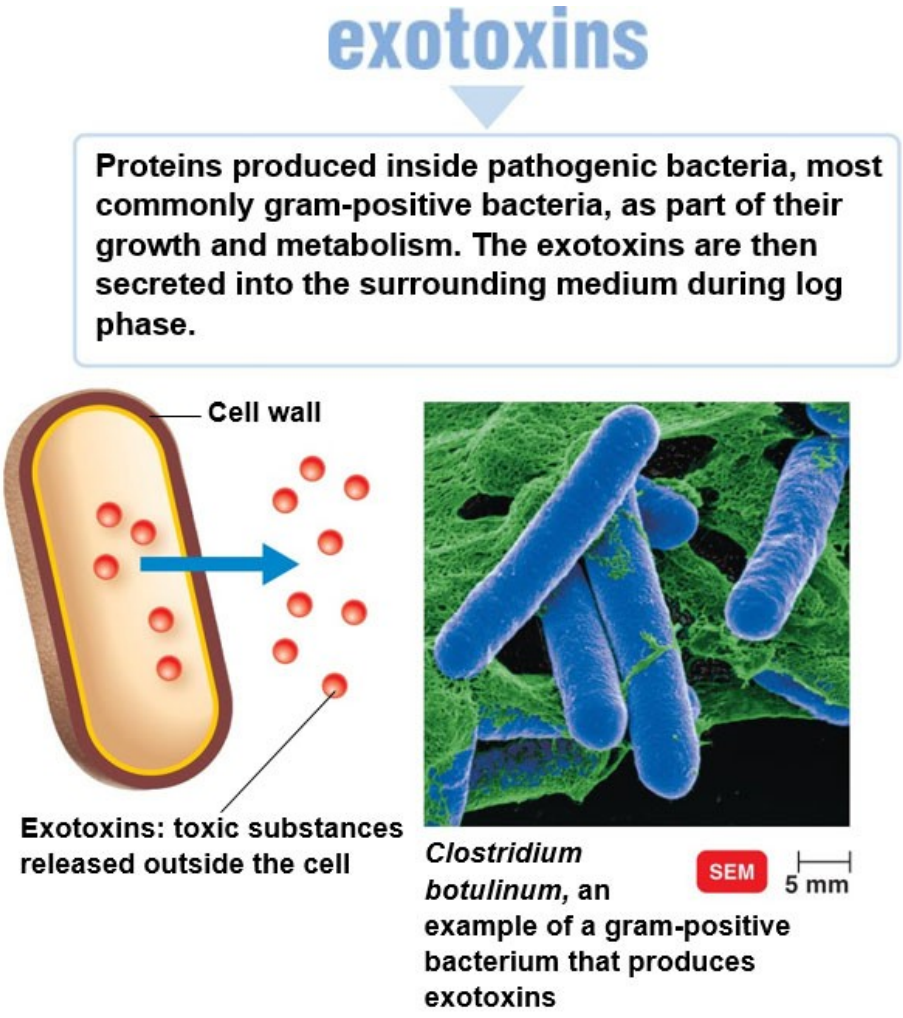
Figure 15.4 Mechanisms of Exotoxins and Endotoxins (1 of 2)



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Virulence Factors: Exotoxins

Animation: Virulence Factors: Exotoxins

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Exotoxins (2 of 6)

- **A-B toxins** contain an enzyme component (A part) and a binding component (B part)
  - Diphtheria toxin

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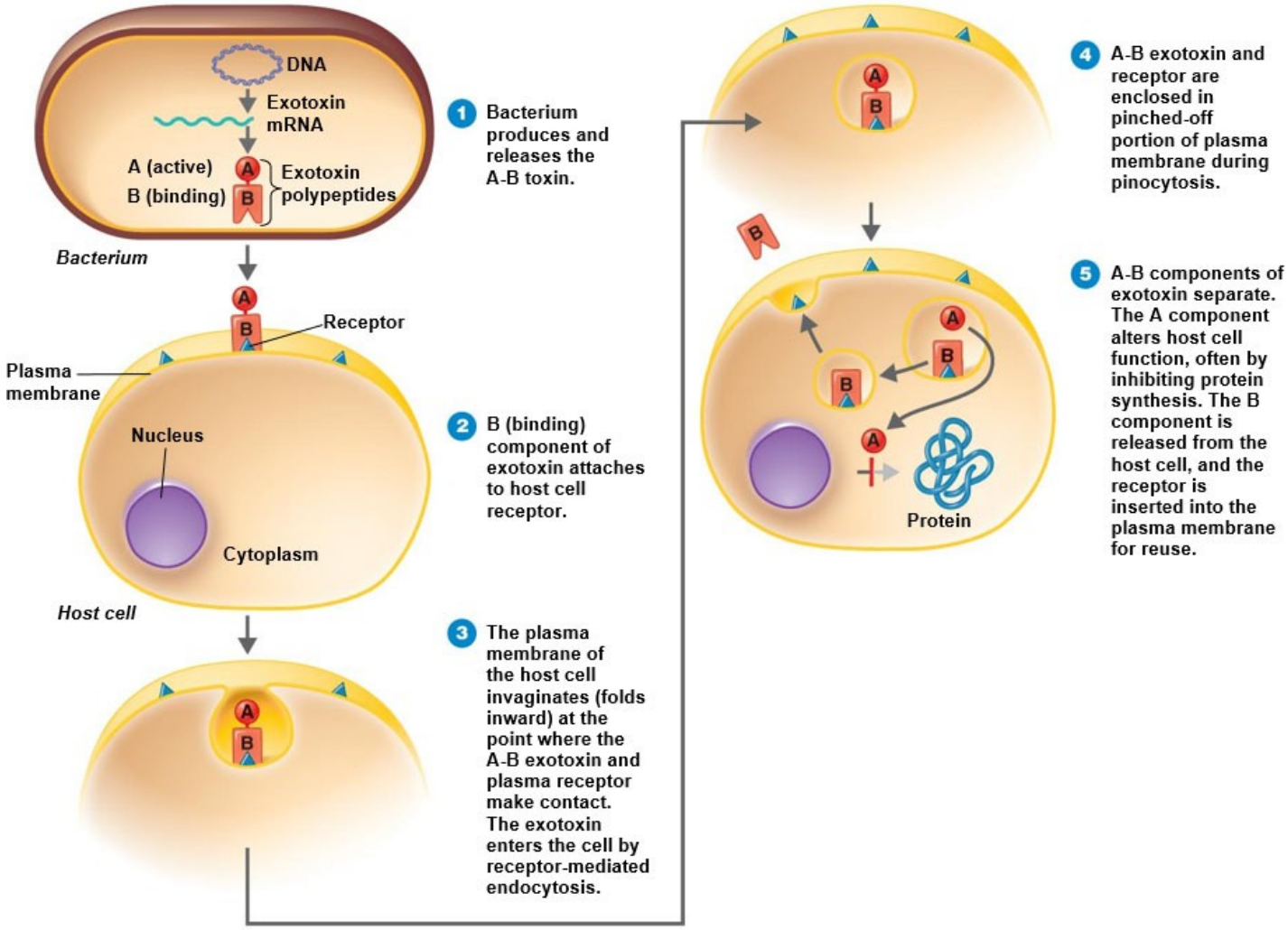
Figure 15.5 The Action of an A-B Exotoxin



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Exotoxins (3 of 6)

- **Membrane-disrupting toxins** lyse host cells by disrupting plasma membranes
  - **Leukocidins**—kill phagocytic leukocytes
  - **Hemolysins**—kill erythrocytes by forming protein channels
  - **Streptolysins**—hemolysins produced by streptococci

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Exotoxins (4 of 6)

- **Superantigens** cause an intense immune response due to release of cytokines from host cells (T cells)
  - Cause symptoms of fever, nausea, vomiting, diarrhea, shock, and death
- **Genotoxins** damage DNA (causing mutations, disrupting cell division, and leading to cancer)

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Table 15.2 Diseases Caused by Exotoxins (1 of 2)

Disease	Bacterium	Type of Exotoxin	Mechanism
Botulism	**Clostridium botulinum**	A-B	Neurotoxin prevents transmission of nerve impulses; flaccid paralysis results.
Tetanus	**Clostridium tetani**	A-B	Neurotoxin blocks nerve impulses to muscle relaxation pathway; results in uncontrollable muscle contractions.
Diphtheria	**Corynebacterium diphtheriae**	A-B	Cytotoxin inhibits protein synthesis, especially in nerve, heart, and kidney cells.
Scalded skin syndrome	**Staphylococcus aureus**	A-B	One exotoxin causes skin layers to separate and slough off.
Cholera	**Vibrio cholerae**	A-B	Enterotoxin causes secretion of large amounts of fluids and electrolytes that result in diarrhea.
Traveler's diarrhea	Enterotoxigenic **Escherichia coli** and **Shigella** spp.	A-B	Enterotoxin causes secretion of large amounts of fluids and electrolytes that result in diarrhea

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Table 15.2 Diseases Caused by Exotoxins (2 of 2)

Disease	bacterium	Type of Exotoxin	Mechanism
Anthrax	**Bacillus anthracis**	A-B	Two a components enter the cell via the same B. the a proteins cause shock and reduce the immune response.
Gas gangrene and food poisoning	**Clostridium perfringens and other species of Clostridium**	Membrane-disrupting	One exotoxin (cytotoxin) causes massive red blood cell destruction (hemolysis); another exotoxin (enterotoxin) is related to food poisoning and causes diarrhea.
Antibiotic-associated diarrhea	**Clostridium difficile**	Membrane-disrupting	Enterotoxin causes secretion of fluids and electrolytes that results in diarrhea; cytotoxin disrupts host cytoskeleton.
Food poisoning	**Staphylococcus aureus**	Superantigen	Enterotoxin causes secretion of fluids and electrolytes that results in diarrhea.
Toxic shock syndrome (TSS)	**Staphylococcus aureus**	Superantigen	Toxin causes secretion of fluids and electrolytes from capillaries that decreases blood volume and lowers blood pressure.
Stomach	**Helicobacter**		toxin causes breaks in eukaryotic

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Endotoxins (5 of 6)

- **Lipid A** portion of lipopolysaccharides (LPS) of gram-negative bacteria
- Released during bacterial multiplication and when gram-negative bacteria die
  - Stimulate macrophages to release cytokines
  - Cause disseminated intravascular coagulation

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Figure 15.4 Mechanisms of Exotoxins and Endotoxins (2 of 2)

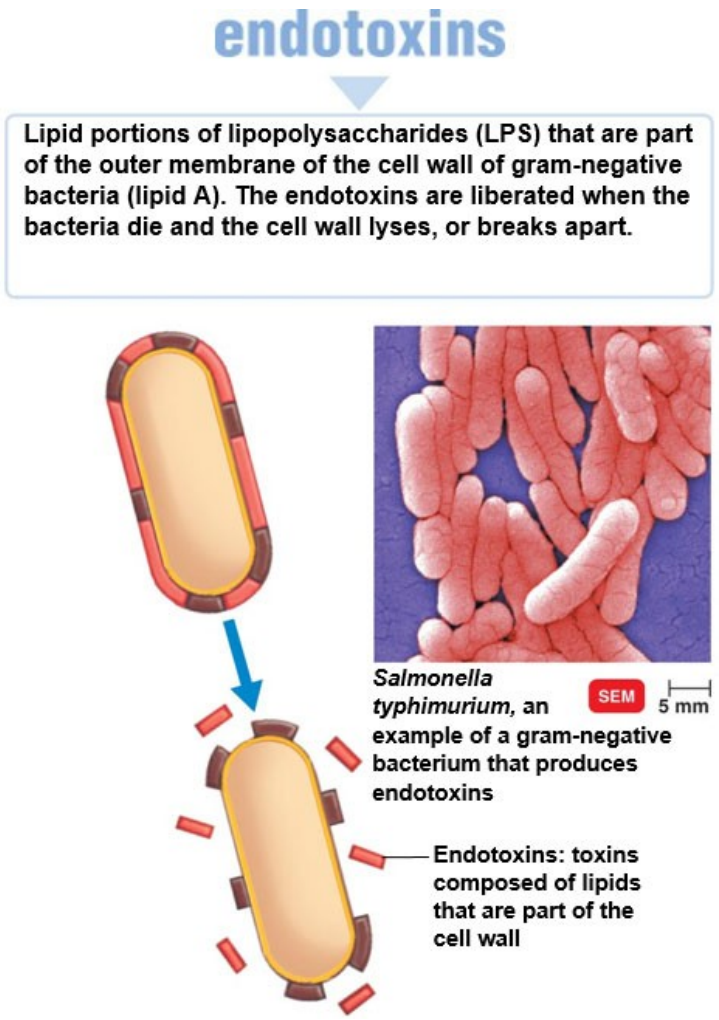

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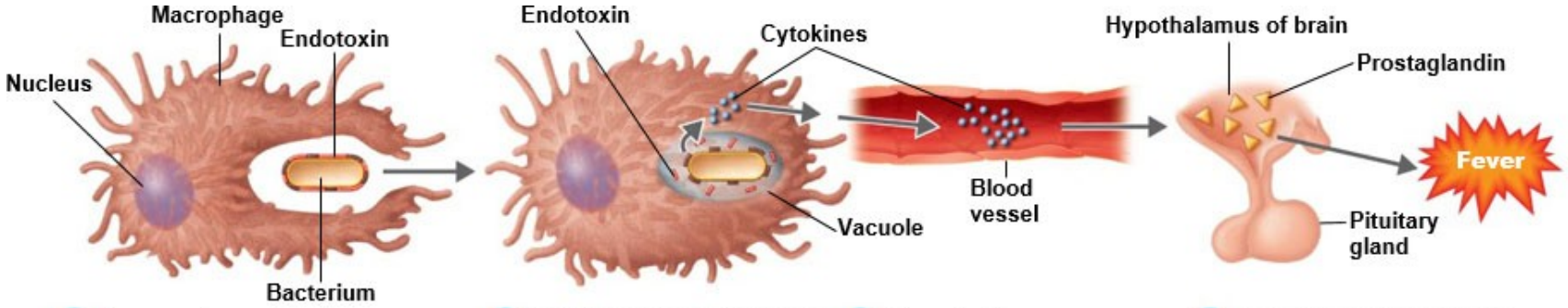
Figure 15.6 Endotoxins and the Pyrogenic Response



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Endotoxins (6 of 6)

- **Limulus amebocyte lysate (LAL) assay** is used to test for endotoxins
  - Blood of horseshoe crabs contains amebocytes
  - Amebocytes lyse in the presence of endotoxin, producing a clot

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Virulence Factors: Endotoxins

Animation: Virulence Factors: Endotoxins

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Table 15.3 Exotoxins and Endotoxins (1 of 2)

Table 15.3 Exotoxins and Endotoxins

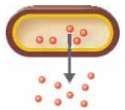
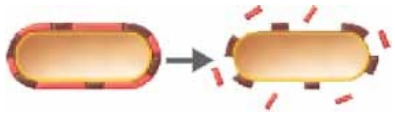
Property	Exotoxins	Endotoxins
		
Bacterial Source	Mostly from gram-positive bacteria	Gram-negative bacteria
Relation to Microorganism	Metabolic product of growing cell	Present in LPS of outer membrane of cell wall and released with destruction of cell or during cell division
Chemistry	Proteins, usually with two parts (A-B)	Lipid portion (lipid A) of LPS of outer membrane (lipopolysaccharide).
Pharmacology (Effect on Body)	Specific for a particular cell structure or function in the host (mainly affects cell functions, nerves, and gastrointestinal tract)	General, such as fever, weaknesses, aches, and shock; all produce the same effects

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Table 15.3 Exotoxins and Endotoxins (2 of 2)

Table 15.3 Exotoxins and Endotoxins

Property	Exotoxins	Endotoxins
Heat stability	Unstable; can usually be destroyed at 60–80°C (except staphylococcal enterotoxin)	Stable; can withstand autoclaving (121°C for 1 hour)
Toxicity (ability to Cause Disease)	High	Low
Fever-Producing	No	Yes
Immunology (relation to antibodies)	Can be converted to toxoids to immunize against toxin; neutralized by antitoxin	Not easily neutralized by antitoxin; therefore, effective toxoids cannot be made to immunize against toxin
Lethal Dose	Small	Considerably larger
Representative Diseases	Gas gangrene, tetanus, botulism, diphtheria, scarlet fever	Typhoid fever, urinary tract infections, and meningococcal meningitis

Reserved

Plasmids, Lysogeny, and Pathogenicity

- Plasmids may carry genes for toxins, production of antibiotics, and enzymes
- **Lysogenic conversion** changes characteristics of a microbe due to incorporation of a prophage

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Check Your Understanding-3

Check Your Understanding

- ✓ Of what value are siderophores?
  15-8
- ✓ How does toxigenicity differ from direct damage?
  15-9
- ✓ Differentiate an exotoxin from an endotoxin.
  15-10
- ✓ Food poisoning can be divided into two categories: food infection and food intoxication. On the basis of toxin production by bacteria, explain the difference between these two categories.
  15-11

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Check Your Understanding-4

Check Your Understanding

- ✓ Washwater containing **Pseudomonas** was sterilized and used to wash cardiac catheters. Three patients developed fever, chills, and hypotension following cardiac catheterization. The water and catheters were sterile. Why did the patients show these reactions? How should the water have been tested?
  15-12
- ✓ How can lysogeny turn the normally harmless **E. coli** into a pathogen?
  15-13

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Pathogenic Properties of Viruses (1 of 2)

Learning Objective

15-14 List nine cytopathic effects of viral infections.

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Pathogenic Properties of Viruses (2 of 2)

- **Cytopathic effects (CPE)** are visible effects of viral infection on a cell
  - Stopping cell synthesis
  - Causing cell lysosomes to release enzymes
  - Creating **inclusion bodies** in the cell cytoplasm
  - Fusing cells to create a **syncytium**
  - Changing host cell function or inducing chromosomal changes
  - Inducing antigenic changes on the cell surface
  - Loss of **contact inhibition** in the cell, leading to cancer
  - Producing **interferons** to protect uninfected cells

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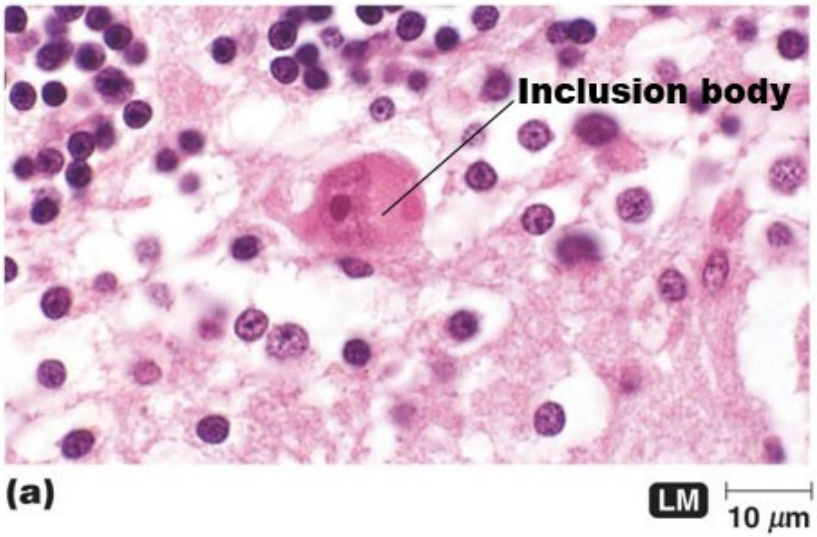
Figure 15.7 Some Cytopathic Effects of Viruses



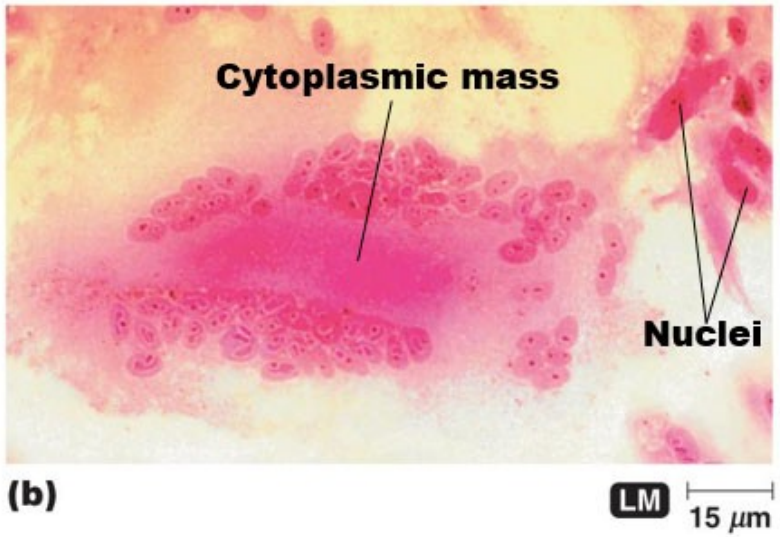


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Figure 15.8 Human Fibroblasts Are Transformed by Rous Sarcoma Virus

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Check Your Understanding-5

Check Your Understanding

- ✓ Define **cytopathic effects**, and give five examples. 15-14

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Pathogenic Properties of Fungi, Protozoa, Helminths, and Algae

Learning Objective

15-15 Discuss the causes of symptoms in fungal, protozoan, helminthic, and algal diseases.

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Fungi (1 of 2)

- Toxic metabolic products
- Provoke an allergic response
- Trichothecene toxins inhibit protein synthesis
- Proteases modify host cell membranes
- Capsules prevent phagocytosis

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Fungi (2 of 2)

- **Ergot** are alkaloid toxins that cause hallucinations
- **Aflatoxin** is a carcinogenic toxin produced by **Aspergillus**
- **Mycotoxins** are produced by mushrooms and are neurotoxic
  - **Phalloidin** and **amanitin**

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Protozoa

- Presence of protozoa and their waste products causes symptoms
- Avoid host defenses by:
  - Digesting cells and tissue fluids
  - Growing in phagocytes
  - Antigenic variation

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Helminths

- Use host tissue for growth
- Produce large masses; cause cellular damage
- Produce waste products
- Produce waste products that cause symptoms

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Algae

- Some produce a neurotoxin called **saxitoxin**
  - Paralytic shellfish poisoning

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Check Your Understanding-6

Check Your Understanding

- ✓ Identify one virulence factor that contributes to the pathogenicity of each of the following: fungi, protozoa, helminths, and algae.
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Portals of Exit (1 of 2)

Learning Objective

15-16 Differentiate portal of entry and portal of exit.

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Portals of Exit (2 of 2)

- Respiratory tract
  - Coughing and sneezing
- Gastrointestinal tract
  - Feces and saliva
- Genitourinary tract
  - Urine; secretions from the penis and vagina
- Skin
- Blood
  - Arthropods that bite; needles or syringes

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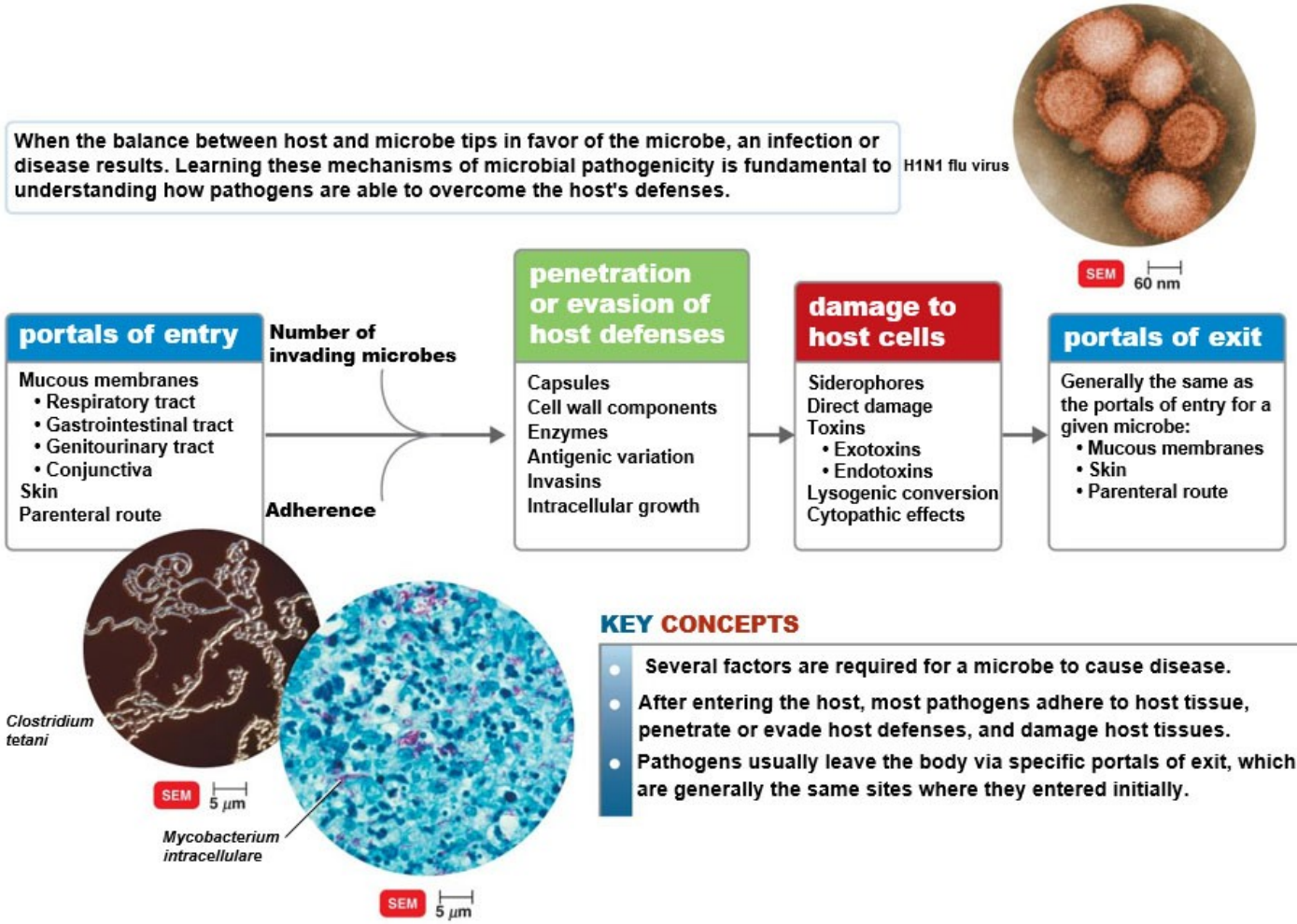
Figure 15.9 Microbial Mechanisms of Pathogenicity



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Check Your Understanding-7

Check Your Understanding

- ✓ Which are the most often used portals of exit? 15-16

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